REMARKS

Following entry of the above amendments, the Examiner is respectfully requested to withdraw all of the remaining rejections and allow Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84, the only claims pending and currently under examination in this application following entry of the above amendments.

Claims 50, 58, 59, 60, 62, 63, 64, 66, 67 and 71 have been amended to clarify that the collection of features includes at least on hybridization feature and at least one background feature, and that the two features are distinct types of features in the collection, as supported by the description of hybridization features and background features in the specification. See e.g., page 4, lines 7-21. Furthermore, Claims 58, 66 and 62 have been amended to clarify that the background probe nucleic acids are those appearing in seq id nos 5 to 18 and 24 to 32, support for these amendments being found in the specification at, among other locations, the originally filed Claims 16 to 18. As the above amendments introduce no new matter, their entry by the Examiner is respectfully requested.

The specification is objected to on the grounds that documents have been improperly incorporated by reference. The Examiner objects to the language at page 8, lines 28-29 relating to relating to the incorporation by reference of all patents, patent applications and publications mentioned in the application. The Examiner asserts that the language "fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited references." The Applicants note that the documents cited in the instant application are incorporated by reference in their entirety and are not limited to specific portions or passages thereof.

In making this objection, the Examiner relies on *Advanced Display Systems*. As is demonstrated below, the Applicants respectfully submit that the cited case law cited in the Office Action is mischaracterized and does not, in fact, stand for the

general principle alleged in the Office Action. Accordingly, the Applicants thus respectfully submit, as supported by the discussion below, that the instant situation is not analogous to that of *Advanced Display Systems, Inc*. Furthermore, the Applicants respectfully submit that the manner in which the documents of the instant application are incorporated by reference are proper and thus the documents cited in the present application are properly incorporated by reference in their entireties.

The Office Action relies on *Advanced Display Systems, Inc.*, to support a general proposition that the specification must identify specific portions of a document incorporated by reference. The relevant issue in *Advanced Systems* concerned anticipation based not on a patent alone, but rather on the combination of the patent and the material potentially incorporated by reference therein. The issue thus was whether a magistrate judge committed legal error by instructing the jury to determine whether and what material was incorporated by reference into the patent. The court described generally the subject of incorporation by reference. In this description, the court noted " To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents. See In re Seversky, 474 F.2d 671, 674, 177 U.S.P.Q. (BNA) 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found")". It is this passage that the Office Action cites.

However, the situation of *In re Seversky*, the case cited in *Advanced Display*, is wholly different from the present situation. In the situation of **In re Seversky**, the Appellant attempted to incorporate by reference teachings of interest from a grandparent application. The parent application, was totally devoid of any reference to the teachings of interest, however the Appellant urged that the defect was cured because the grandparent disclosed the teachings and because the parent application is a continuation-in-part of the grandparent that disclosure was, ipso facto, incorporated by reference in the parent. In other words, the situation was one in which there was no "incorporation-by-reference" language whatsoever - a situation wholly different from the instant application which does include "incorporation-by-reference" language.

Accordingly, the Applicants submit that the documents cited in the instant application are properly incorporated by reference in their entireties. As such, the Applicants respectfully request the objection to the specification be withdrawn.

Next, Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84 have been rejected under 35 U.S.C. § 112, ¶ for an asserted lack of written description.

In making this rejection, the Examiner asserts in paragraph 6 of the office action that the claim reads such that hybridization feature includes within it a background feature, and questions how this can be in view of the cited passages of the specification which described the two types of features as distinct from each other. It is respectfully submitted that the claims prior to the above amendments were clear in that the collection features includes at least one background feature, and no where did the claim language imply that a hybridization feature include within it a background feature. Nonetheless, in order to further expedite the prosecution of the present application, the claims have been amended to clarify that the collection of features includes at least one hybridization feature and at least one background feature.

In paragraph 7 of the office action, the Examiner asserts that the minimum number of exemplary background probes is not sufficient in view of the specification at page 16, lines 15 to 20 which states:

> In a preferred embodiment, a background feature contains 3.1×10^6 to 6.3×10^7 background probes, preferably 1.6×10^7 to 4.7×10^7, more preferably 2.8×10^7 to 3.5×10^7 background probes.

However, this section is speaking about the number of individual nucleic acid molecules that are present in a given background feature of a collection, not the total number of different background features that must be present in a given collection. As such, the specification need not disclose 3.1×10^6 different background probe sequences in order to comply with written description, since this teaching of the specification is referring to the number of different (identical) molecules that are

present in a given background feature, not the number of different background features that must be present in a given collection.

Furthermore, in paragraph 7 the Examiner questions the specification with respect to certain seq id nos, since they are longer than the recited length for background probes in the specification but nonetheless recited in certain of the claims as background features. In view of the above amendments to the claims, this particular issue is addressed.

In view of the above, it is submitted that the claims do comply with the written description requirement in that the claims are directed to methods of performing array assays with arrays that include background features and hybridization features, where the signals from background features are subtracted from the signals from hybridization features. The specification provides multiple representative examples, including working examples, of representative background features being employed in the claims methods, such that one of skill in the art would have no doubt that the applicant was in possession of the invention as claimed at the time the application was filed.

Next, Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84 remain rejected under 35 U.S.C. § 103 (a) as being unpatentable over Dehlinger in view of Fodor, Blanchard and Brink, and further in view of Iitiä.

In making this rejection, the Examiner asserts that since Dehlinger suggests the use of negative control probes, Fodor and Blanchard disclose arrays of all possible oligomers of the lengths of probes of the present invention, Brink discloses the use of type I and type II control sequences that are designed to not hybridize to a target, and Iitiä assertedly teaches sequences that do not specifically hybridize to their complement, the subject claims are obvious.

However, it is respectfully submitted that the combined teachings of the references fail to teach or suggest at least the following element of the claims.

As can be seen from Claims 50-57, 60-61 and 64-65 (as well an any dependent claims thereon), the background feature of the claims is one that does not hybridize to its fully complementary target nucleic acid under stringent conditions, where the target nucleic acid is one that is fully complementary to the probe and therefore would be expected to hybridize to the probe. As such, but for the empirical observation that the probe does not actually bind to its fully complementary target, one would expect the probe to bind to its target.

None of the references teach or suggest, either alone or in combination, such a probe as a background probe. In fact, all of the mentioned negative control probe sequences in the cited references are ones that, based on known structure and sequence, are expected not to bind to their corresponding targets. For example, the type I probes in Brink are ones that are identical in sequence to their target but of opposite polarity. Prior to actual testing, such a sequence would be known not to hybridize to its corresponding target. Similarly, Brink's Type II probe is one that has the complementary sequence to its target but has the same polarity, i.e., the two sequences are complementary only if they are lined up or paired in the same direction, i.e., 5' to 3'. For example, where a target sequence in Brink is 5'-ATCG-3', the Brink Type II probe would have a sequence 5'-TAGC-3'. When these complementary strands of the same polarity are aligned, one obtains:

5'-ATCG-3'

3'-CGAT-5'

which clearly do not hybridize to each other. Again, prior to actual testing, such a sequence would be known not to hybridize to its target.

In contrast, the background probes of these presently pending claims are ones that are empirically observed to not hybridize to their targets, where but for the empirical testing, they would be expected to hybridize to their targets under stringent conditions.

With respect to Claims 58, 62 and 66 (as well as the claims dependent thereon), these claims require the presence of specific sequences as background features, i.e., one or more of SEQ ID NOs: 05-18 and 24-32. Nothing in the cited

references teaches or suggests that one must include these specific sequences. While Blanchard and Fodor may suggest a large number of sequences, there is no guidance in these references, or any of the other references, to select any of specific sequences 05-18 or 24-32. Therefore the combined teachings of these references fails to teach or suggest these claims.

Claims 59, 63 and 67 (and any claims dependent thereon) limit the background probes to ones that have specific characteristics, e.g., reverse polarity nucleotide analogs, etc. The Examiner has not pointed to any location in the cited references where these specific characteristics are disclosed or suggested. Accordingly, the combined teaching of the references fails to teach or suggest these claims.

Finally, Claim 71 and the claims dependent thereon recite that the background feature must be a probe that does not hybridize to any target in the sample being assayed. The cited references teach the use of control probes that do not hybridize to the target for which they are designed, but one can envision target nucleic acids to which they would hybridize. For example, even though the type I and type II probes of Brink will not hybridize to the specific targets for which they are designed, one can envision target nucleic acids to which they would bind. As such, the combined teachings of the reference fail to render these claims obvious as well.

Finally, Iitiä fails to make up the above deficiencies for the following reasons. Iitiä has been cited by the Examiner as assertedly teaching probes that do not hybridize to their complementary sequence. However, the cited passage by Iitiä actually states:

"We repeatedly obtained lower hybridization signal with the probes designed against the sense strand of the target DNA (probe Eu14M). The reason for this is unknown."

This statement merely states that some probes gave **lower** signal than others, but not that they provide a signal which is representative of background signal such

that the probes could be employed as background probes. Accordingly, Iitiä does not make up the fundamental deficiency in the primary four references as described above.

As such, none of the cited references teach or suggest the claimed invention and the rejection of Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84 as obvious under 35 U.S.C. § 103 (a) as being unpatentable over Dehlinger in view of Fodor, Blanchard and Brink, and further in view of Iitia, may be withdrawn.

Finally, Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting over claims 13 and 15-23 of copending application serial no. 09/899,381. In view of the enclosed Terminal Disclaimer, this rejection may be withdrawn.

Conclusion

The Applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 833-7770 or Gordon Stewart at (650) 485-2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: 8·9·04

By: _____
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enc:

- Terminal Disclaimer over application no. 09/899,381